

Amendments to the Claims

Prior to substantive examination, Applicant has cancelled claims 1-59 without prejudice to their subsequent reintroduction into this application or their introduction into a related application. New claims 60-80 have been added. The following list of claims replaces all prior versions and lists of claims in the application.

What is claimed is:

60. (New) A method for identifying a compound capable of promoting deactivation or inhibiting activation of a membrane bound active small GTPase, comprising:

incubating in the presence of a test compound a live cell expressing the membrane bound small GTPase and comprising an active small GTPase specific reporter comprising a small GTPase specific binding moiety and a detectable marker moiety; and,

monitoring association of the reporter with the membrane bound small GTPase, wherein a dissociation of the reporter from the membrane bound small GTPase is indicative that the test compound is capable of promoting deactivation of the membrane bound active small GTPase.

61. (New) The method according to claim 60 wherein the small GTPase is bound to at least one of the plasma membrane, Golgi apparatus membrane, endomembrane, mitochondrial membrane, outer nuclear membrane, inner nuclear membrane, endoplasmic reticulum, sarcoplasmic reticulum, a membrane of transport, and secretory vesicles.

62. (New) The method according to claim 60 wherein the membrane bound small GTPase is a Ras superfamily GTPase.

63. (New) The method according to claim 60 wherein the membrane bound small GTPase is a Ras, Rho, Ran, Arf/Sar1, or Rab/YPT1 subfamily GTPase.

64. (New) The method according to claim 60 wherein the small GTPase is a hyperactive or a constitutively active mutant small GTPase.
65. (New) The method according to claim 60 wherein the small GTPase is a Ras.
66. (New) The method according to claim 60 wherein the membrane bound small GTPase is one or more Ras GTPase, selected from the group consisting of H-Ras, K-Ras and N-Ras.
67. (New) The method according to claim 60 wherein the small GTPase is a hyperactive or oncogenic Ras.
68. (New) The method according to claim 60 wherein the small GTPase specific binding moiety is a peptide derived from an effector of the small GTPase.
69. (New) The method according to claim 60 wherein the small GTPase specific binding moiety is a peptide derived from an effector of the small GTPase having one or more point mutations that increase the affinity of the peptide for the small GTPase relative to the affinity of the wild type effector for the small GTPase.
70. (New) The method according to claim 60 wherein the small GTPase is a Ras and the small GTPase-specific binding moiety is an active-Ras-specific-binding moiety.
71. (New) The method according to claim 70 wherein the active-Ras specific binding moiety is Raf-1-RBD, or a derivative thereof.
72. (New) The method according to claim 60 wherein the reporter is a reporter protein.
73. (New) The method according to claim 60 wherein the detectable marker moiety is selected from a luminescent protein and a fluorescent protein.

74. (New) The method according to claim 73 wherein monitoring is performed by fluorescence microscopy.
75. (New) The method according to claim 73 wherein monitoring is performed by fluorescence microscopy using a method selected from the group consisting of wide-field fluorescence microscopy, total internal reflection fluorescence microscopy, fluorescence lifetime imaging and confocal imaging.
76. (New) The method according to claim 60 wherein the cell is selected from the group consisting of a tumour cell, a primary tumour cell and a cell from an *in vitro* model cell line.
77. (New) A method for identifying a compound capable of promoting deactivation of a membrane bound active Ras, comprising:
incubating in the presence of a test compound a live cell expressing Ras and a specific reporter comprising GFP-RBD or a derivative thereof; and,
monitoring association of the reporter with the membrane bound active Ras,
wherein a dissociation of the reporter from the membrane bound active Ras is indicative that the test compound is capable of promoting deactivation of the membrane bound active Ras.
78. (New) The method according to claim 60 performed in high throughput format.
79. (New) The method according to claim 77 performed in high throughput format.
80. (New) A high throughput screening method for identifying a compound capable of promoting deactivation of a membrane bound active Ras, comprising:
incubating in the presence of a test compound a live cell expressing Ras and a specific reporter comprising GFP-RBD or a derivative thereof; and,
monitoring association of the reporter with the membrane bound active Ras,

wherein a dissociation of the reporter from the membrane bound active Ras is indicative that the test compound is capable of promoting deactivation of the membrane bound active Ras.